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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/431,821    11/02/99    TRECO    D    50010/006006

HM12/0327

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EXAMINER

KETTER, J

ART UNIT

PAPER NUMBER

1636

DATE MAILED:

03/27/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trad marks**

<p align="center"><b>Office Action Summary</b></p>	<p><b>Application No.</b></p> <p>09/431,821</p>	<p><b>Applicant(s)</b></p> <p>TRECO ET AL.</p>	
	<p><b>Examiner</b></p> <p>James Ketter</p>	<p><b>Art Unit</b></p> <p>1636</p>	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 December 2000.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 65-78 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 65-74, 77 and 78 is/are rejected.
- 7) ☒ Claim(s) 75 and 76 is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

- |   |  |
|---|--|
| 15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                  | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 20) <input type="checkbox"/> Other:  |

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This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Claims 75 and 76 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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Claims 65-72, 74, 77 and 78 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 95, 108-120, 135-175, 191-194, 196-210, 213-247, 264-274, 293-303, 317-327, 349-352, 367-370, 383-385, 389-392, 393-395 and 399-403 of copending Application No. 08/406,030. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass the copending claims. With respect to limitation to the recited cell lines, instant claim 66 encompasses copending claims 270, 299 and 323. With respect to limitation to the recited genes, claims 69 and 70 encompass copending claims 108-120. With respect to instant claims 77 and 78, drawn to cells, said claims encompass copending claims 135-175, 213-239, 244-247, 272-274, 301-303, 325-327, 350-352, 368-370, 384, 385, 390-392 and 399-403.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 73, 75 and 76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 95, 108-120, 191-194, 196-210, 238-243, 264-271, 293-300, 317-324, 349, 367, 383, 389 and 393-395 of copending Application No. 08/406,030 in view of Capecchi (Ref. No. 69 on the IDS filed 13 September 2000).

The instant claims are drawn to transfection methods in which the inserted DNA is targeted to a particular locus in the genome using homologous recombination. Negative selection is not specified.

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Capecchi teaches, e.g., beginning at page 1290, the Positive-Negative Selection method, which is taught as useful to enrich the population of transfectant cells for the desired homologous recombinant.

It would have been obvious to one of ordinary skill in the art to have employed the Positive-Negative Selection of Capecchi in combination with the methods of the instant claims. The motivation to have done so would have come from Capecchi, in teaching that the resultant cells are enriched for the desired cells.

This is a provisional obviousness-type double patenting rejection.

Claims 65-68 and 71-78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-10 and 12-24 of U.S. Patent No. 6,063,630 (A). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass the patented claims. With respect to limitation to the recited cell lines, instant claim 66 encompasses copending claim 7. With respect to instant claims 77 and 78, drawn to cells, said claims encompass copending claim 24.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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Claims 65-72, 74, 77 and 78 are rejected under 35 U.S.C. 102(e) as being anticipated by Sherwin et al. (B).

Sherwin et al. teaches, methods of transfecting cells with DNA constructs which comprise a targeting (i.e., homology) sequence and an regulatory sequence. The target genes may be one of a large number recited, broadly being hormone, cytokine, antigen, antibody, enzyme, clotting factor, transcription factors, receptors or regulatory proteins, specifically including insulin, erythropoietin, growth hormone or factor VIII and so forth. The constructs are also claimed as comprising a selectable marker. Also claimed are cells resulting from this method.

Sherwin et al. teaches homologous recombination in primary cells from mammals. Sherwin et al. claims priority back to, and incorporates by reference, 07/432,069, filed 11/6/89. The Sherwin et al. patent is ultimately a CIP of 07/432,069, and has thus summarized some of the teachings thereof. Unfortunately, under 37 CFR § 1.14, the Examiner may not set forth quotations from 07/432,069 directly, nor provide a copy thereof. Applicants are advised to review 37 CFR § 1.14 for conditions under which they might obtain access to 07/432,069. At column 2, at the "SUMMARY OF THE INVENTION", Sherwin et al. teaches that a gene may be targeted (using homologous recombination) for integration by a DNA sequence which causes expression of said gene. The 07/432,069 application expands this disclosure to include teachings that the targeting DNA may be upstream, at the regulatory elements, as far as 25, 50 or 100 kb away, or in the coding or downstream regions. One or more regulatory elements were taught to be included. Also taught were use of any combination of introns and exons. Introduction of mutations is taught as well, which would alter the expression of the gene. Such is noted in

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Sherwin et al., e.g., at the paragraph bridging columns 5 and 6. 07/432,069 teaches expression of the thus targeted gene, as well as detection of the resultant protein, as well as use of primary cells or immortalized cells as the target cells. With respect to the target gene, 07/432,069 teaches numerous types of genes and specific genes. Among others, erythropoietin and insulin and clotting factors are taught. 07/432,069 broadly discloses that any gene of interest may be a potential target.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 65, 72 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherwin et al. (B) in view of Capecchi (69).

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The invention is drawn to a method of transfecting cells with DNA constructs which comprise a targeting (i.e., homology) sequence and a regulatory sequence, and wherein said construct possesses a positive and a negative selection marker.

Sherwin et al. is described, supra. Sherwin et al. differs from the claimed invention in not teaching the use of a negative selection marker in combination with the positive selection marker.

Capecchi teaches, e.g., beginning at page 1290, the Positive-Negative Selection method, which is taught as useful to enrich the population of transfectant cells for the desired homologous recombinant.

It would have been obvious to one of ordinary skill in the art to modified the methods taught by Sherwin et al. to have employed the Positive-Negative Selection of Capecchi. The motivation to have done so would have come from Capecchi, in teaching that the resultant cells are enriched for the desired cells.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993)(see 37 CFR § 1.6(d)). The Art Unit 1636 Fax number is (703) 305-7939. NOTE: If Applicant *does* submit a paper by fax to this number, the examiner must be notified promptly, to ensure matching of the faxed paper to the application file, and the original signed copy should be retained by Applicant or Applicant's representative. (703) 308-4242 or (703) 305-3014 may be used without



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notification of the examiner, with such faxed papers being handled in the manner of mailed responses. Applicants are encouraged to use the latter two fax numbers unless immediate action by the examiner is required, e.g., during discussions of claim language for allowable subject matter. **NO DUPLICATE COPIES SHOULD BE SUBMITTED** so as to avoid the processing of duplicate papers in the Office.

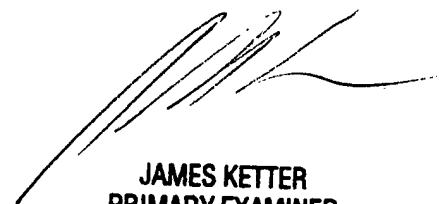
Any inquiry concerning this communication or earlier communications from the examiner with respect to the examination on the merits should be directed to James Ketter whose telephone number is (703) 308-1169. The examiner can normally be reached on M-F (9:00-6:30) Alternate Fridays Off.

Questions regarding formalities and processing of the case should be directed to Zeta Adams, whose telephone number is (703) 305-3291.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, John LeGuyader, can be reached at 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234.

jsk  
March 24, 2001



**JAMES KETTER  
PRIMARY EXAMINER**